

## Replication of Mycobacterium tuberculosis in retinal pigment epithelium.

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### Public Summary:

Tuberculosis is an important cause of severe eye inflammation that can lead to blindness; but, the pathways by which eye harbors tuberculosis bacteria are not clear. There are evidences showing that tuberculosis bacteria can remain dormant within specific cell types in the eye and become reactivated later in life. In this study, we showed, for the first time, that tuberculosis bacteria can get into the retinal pigmented epithelium cells and proliferate slowly inside these cells without killing them. The mechanisms by which tuberculosis bacteria enter retinal pigment epithelium cells and bacteria proliferation rate are compared to those in immune system cells.

### Scientific Abstract:

**IMPORTANCE:** Mycobacterium tuberculosis is an important cause of posterior uveitis in tuberculosis-endemic regions. Clinical and histopathologic evidence suggests that retinal pigment epithelium (RPE) can harbor M tuberculosis. However, the mechanism of M tuberculosis phagocytosis and its growth in RPE is not clear. **OBJECTIVE:** To investigate M tuberculosis phagocytosis, replication, and cytopathic effects in RPE cells compared with macrophages. **DESIGN, SETTING, AND PARTICIPANTS:** Human fetal RPE and monocytic leukemia macrophage (THP-1) cell lines were cultured, and RPE and THP-1 cells were exposed to avirulent M tuberculosis H37Ra. Mycobacteria were added to RPE and THP-1 cells with a 5:1 multiplicity of infection. Nonphagocytized M tuberculosis was removed after 12 hours of exposure (day 0). Cells were harvested at days 0, 1, and 5 to count live and dead cells and intracellular mycobacteria. Toll-like receptor 2 (TLR2) and TLR4 expression was determined by immunohistochemistry; intracellular bacillary load, following TLR2 and TLR4 blockade. **MAIN OUTCOMES AND MEASURES:** Number of intracellular M tuberculosis, cell survival, and TLR2 and TLR4 expression in RPE and THP-1 cells following exposure to M tuberculosis. **RESULTS:** At day 0, an equal number of intracellular M tuberculosis was observed per THP-1 and RPE cells (0.45 and 0.35 M tuberculosis per RPE and THP-1 cells, respectively). Mean (SD) number of intracellular M tuberculosis at day 5 was 1.9 (0.03) and 3.3 (0.01) per RPE and THP-1 cells, respectively ( $P < .001$ ). Viability of infected RPE was significantly greater than that of THP-1 cells at day 5 (viable cells: 17 [8%] THP-1 vs 73% [4%] RPE;  $P < .05$ ). Expression of TLR2 and TLR4 was detected in both cell types after 12 hours of exposure. Inhibition of TLR2 and TLR4 reduced intracellular M tuberculosis counts in RPE but not in THP-1 cells. **CONCLUSIONS AND RELEVANCE:** Mycobacterium tuberculosis is phagocytized by RPE to a similar extent as in macrophages. However, RPE cells are better able to control bacillary growth and RPE cell survival is greater than that of THP-1 cells following mycobacterial infection, suggesting that RPE can serve as a reservoir for intraocular M tuberculosis infection.

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